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# Not all shock states are created equal: a review of the diagnosis and management of septic, hypovolemic, cardiogenic, obstructive, and distributive shock

Sarah Khorsand, MD, FASA[1] ;Mada F Helou, MD[2] ; Veena Satyapriya, MD[3] ; Rafal Kopanczyk, DO[3] ; Ashish K Khanna, MD, MS, FCCP, FCCM, FASA [4,5,6]

1 Department of Anesthesiology and Pain Management, University of Texas at Southwestern Medical Center, Dallas TX

2 Department of Anesthesiology and Perioperative Medicine, University Hospitals, Cleveland Medical Center, Cleveland, OH

3 Department of Anesthesiology, The Ohio State University Wexner Medical Center, Columbus, OH

4 Department of Anesthesiology, Wake Forest University School of Medicine, Atrium Health Wake Forest Baptist, Winston-Salem, NC

5 Perioperative Outcomes and Informatics Collaborative (POIC), Winston-Salem, NC

6 Outcomes Research Consortium, Cleveland, OH

Address correspondence to: Ashish K Khanna, M.D., Associate Professor and Vice-Chair for Research, Department of Anesthesiology, Section on Critical Care Medicine, Wake Forest Baptist Medical Center, 1 Medical Center Blvd, 9th Floor Janeway Tower, Winston-Salem, NC 27157. Tel: 513-658-5866, Fax:336-716-8190 Email: akhanna@wakehealth.edu.

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**Abstract:**

Shock is commonplace in the intensive care unit (ICU) and is associated with poor outcomes. Classically, shock is divided into the following categories: distributive, hypovolemic, obstructive, and cardiogenic, of which distributive (and usually septic distributive) is by far the most common. Clinical history, physical examination, and hemodynamic assessments help differentiate shock states. Specific management necessitates interventions to correct the triggering etiology as well as ongoing resuscitation to maintain physiological milieu. One shock state may convert to another and may have an undifferentiated presentation as well, therefore continual re-assessment is essential. This review provides guidance for anesthesiologists and intensivists on the assessment and management of all shock states based on expert opinion and scientific evidence where available.

**Keywords:** Shock; diagnosis; management; intervention; types

**Key points:**

1. Shock is a common entity present in up to a third of all critical care patients

2. Clinical history and physical examination may help differentiate type of shock. Assessment of relevant hemodynamic variables, such as blood pressure, heart rate, cardiac output, filling pressures, systemic vascular resistance, measures of flow or perfusion, and oxygen extraction further assist in diagnosis and management. Point-of-care ultrasound is routinely used in early assessment of shock.

3. Specific management of shock states involves correction of the triggering etiology and goal-directed resuscitation.

4. One shock state may convert to another or may have an undifferentiated presentation; therefore, frequent re-assessment is necessary.

## Introduction

The characteristic definition of circulatory shock is the combination of hypotension and hypoperfusion that amounts to progressive failure of oxygen utilization at the cellular level and organ system failure. Shock remains one of the most common causes of emergent intensive care admission across the world.[1] Typical pathophysiological variants of shock are most commonly distributive or vasodilatory followed by cardiogenic, hypovolemic, and obstructive (Table 1 and Figure 1). Mixed shock, specifically sepsis or septic vasodilatory shock in the setting of pre-existent cardiogenic shock is associated with worse outcomes.[2,3] Whatever the etiology, both short-term and long-term organ dysfunction secondary to shock comes with high mortality for the patient and a substantial economic burden to any healthcare system.[4] This review evaluates types of shock divided into the traditional pathophysiological categories and provides evidence-based guidance for the treatment and management of each.

### Evolution of Shock Management

The last decade has witnessed an exponential growth in available literature specific to resuscitation targets and hemodynamic thresholds of shock. An investigation of nearly 9,000 critically ill patients across several ICU systems in the United States identified the earliest increased risk of myocardial injury, acute kidney injury, and mortality at a mean arterial pressure of 85 mmHg.[5] Another investigation of several thousand postoperative intensive care patients identified a non-linear increase in myocardial injury and mortality at pressures higher than the traditional norm of 65 mmHg.[6] A multicenter, randomized trial of 424 with septic shock determined that a resuscitation strategy targeting normalization of capillary refill time, compared with a strategy targeting serum lactate levels, did not reduce all-cause 28-day mortality.[7]

The role of continuous noninvasive and minimally invasive monitoring for shock is in a state of rapid evolution. New, well-validated measurement techniques are able to complement traditional measures such as the pulmonary artery catheter (PAC).[8] In addition, the use of mechanical circulatory support devices and extracorporeal systems to manage various degrees of cardiogenic shock has rapidly increased worldwide.[2] Further, new vasopressors and increased data for adjuvant therapy and other innovative treatments are available. for shock patients such as steroidsand other innovative therapy to help support organ systems is now available for these patients.[9-11] For example, angiotensin II as an agent to effectively support blood pressure may allow for reduction in other vasopressors and have a substantial survival benefit in the high-renin phenotype of shock.[12,13] Delay in the initiation of vasopressin has been associated with a significant increase in mortality thereby ushering in an era of early and appropriate multimodal use of vasopressors and adjuvants.[14-17] Traditional measures of perfusion such as lactate have been consistently questioned and serum renin has emerged within the limitation of a non-point of care assay as a superior measure of organ perfusion and prognosis in critically ill patients with shock.[18-21]

**Distributive shock**

Vasodilatory or distributive shock is characterized by tissue hypoxemia and low systemic vascular resistance and concomitant high cardiac output and high heart rate.[22] More than 90% of distributive shock is septic shock and usually manifests as a high output state.[23] However, other causes of non-septic vasodilatory shock, including post-cardiopulmonary bypass vasoplegia, anaphylaxis, neurogenic shock, and pancreatitis are important clinically relevant examples. Treatment of distributive shock varies by cause, but usually requires vasoconstrictors, fluids and in some cases may necessitate inotropes as well.

## Septic Shock

### Epidemiology and pathophysiology

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) defined septic shock as a lactate > 2 mmol/L and hypotension requiring vasoconstrictors to maintain MAP > 65 mmHg despite adequate volume resuscitation. Stated otherwise, septic shock is characterized by a life-threatening organ dysfunction caused by dysregulated host response to sepsis resulting in regional hypoxia and mitochondrial dysfunction.[24] The Sepsis-3 taskforce found wide variability in mortality associated with septic shock, from 20% up to 80%, with an average mortality of 40%.[25] Early sepsis may have a subtle presentation, as cardiac output is generally preserved and may be hyperdynamic. Extremities are warm and skin is flushed. Septic shock presents with hypotension, temperature > 38.3° C or < 36° C, tachycardia, and tachypnea. Cardiac output progressively drops as the disease course evolves, with myocardial depression and a low flow state, whereby skin may be mottled with decreased capillary refill. This is more common in patients on prolonged high dose vasopressors, where catecholamine induced myocardial injury and microcirculatory flow impairment is common.[26] Exposure to increasing amounts of catecholamines upwards of 0.8 – 1.0 mcg/kg/min of norepinephrine equivalents may be associated with a 50-80% 30-day mortality.[27,26,28,29] Laboratory work-up demonstrates elevated lactate, and central venous oxygen saturation due to reduced tissue extraction. Where there is clinical equipoise, an elevated procalcitonin may help confirm the presence of sepsis .[30] In non-intensive care settings, a quick-SOFA (qSOFA) score of 2 or more in the presence of altered mental status, respiratory rate > 22/min, or systolic blood pressure < 100 mmHg, portends a poor outcome in the setting of infection.[31]

End-organ dysfunction resulting from septic shock yields myriad conflicting management goals for the intensivist, and these overlap with other shock states. Briefly, acute kidney injury, cardiac demand ischemia, altered mental status, and gut hypoperfusion result from hypoperfusion. Lactic acidosis impairs vascular tone via intracellular signaling and increased expression of nitric oxide synthase. It also causes a decreased responsiveness to endogenous and exogenous catecholamines.[32] Uremia worsens altered mental status and airway protection. Shock liver can make lactate interpretation difficult, as both increased production and decreased clearance will elevate lactate. Septic cardiomyopathy (SCM) is a spectrum of disease, ranging from right and/or left ventricular dilation and dysfunction to myocardial injury and cardiogenic shock, independent of cardiac ischemia. Pathophysiology is likely multifactorial, and pre-existing reduced ejection fraction and coronary artery disease increase the risk of developing SCM during sepsis.[33] Inotropic support for SCM has not been shown to be beneficial, though has not been well-studied in overt sepsis-induced cardiogenic shock. The mixed-shock state this can produce may be better elucidated with the use of a PAC, and the use of temporary mechanical support may be considered.[34]

Diagnosis and Management

Serial tests of end-organ perfusion, such as lactate and central venous oxygenation, assist in diagnosis of septic shock. In addition to standard ICU monitors, patients with rapid decompensation or those who require vasoactive medications benefit from an arterial line.[35] Important clinical endpoints include renal clearance and urine output, mentation, and capillary refill. Monitoring response to a fluid challenge is important to avoid complications of fluid overload. This can be done with continuous monitoring of endpoints such as stroke volume variation (SVV) and pulse pressure variation (PPV).[36] Any change in shock symptomatology

should necessitate re-evaluation for a mixed shock state, with a transthoracic echocardiogram and cardiac biomarkers including troponins, B-type natriuretic peptide (BNP), and N-terminal pro-B-type natriuretic peptide (NT-proBNP).[33]

The management of vasodilatory shock is a step-wise approach (Figure 2). Early initiation of antibiotics and source control is the cornerstone of care for sepsis.[37] Antibiotics should target the suspected infection and address patient risk factors, including prior susceptibilities and resistance and risk of healthcare-acquired pathogens. Source control, medically, surgically or via percutaneous intervention where possible, is vitally important. [38]

Goal-directed therapy should be followed with lactate and central venous oxygen saturation as endpoints of perfusion, as well as improvement in capillary refill time. The importance of continual re-evaluation of volume status and further boluses as needed cannot be over-emphasized. The "ROSE" model of fluid resuscitation in septic shock offered by Malbrain and colleagues emphasizes a four-phase sequence for therapy. The four phases ***R***esuscitation, ***O***ptimization, ***S***tabilization, and ***E***vacuation are to be balanced appropriately while considering the benefits and risks of overdoing any one of these. [39] While and/or once euvolemia is achieved, the use of vasoconstrictors starting with norepinephrine is recommended to maintain adequate end-organ perfusion with a MAP goal of greater than 65 mmHg.[40] Vasopressin may be added as a second agent over escalating doses of norepinephrine. Norepinephrine has stood the test of time as the primary vasopressor for septic shock, though trials comparing this agent with vasopressin as a first-line therapy have not shown a difference in outcomes[41] and may suggest that vasopressin preserves renal function better. [42] Recent evidence has pointed to the detrimental effects of a delay in initiation of vasopressin, being associated with a near 20% increase in mortality for every 10 mcg/min of norepinephrine usage.[15] Understanding the evolution of early

multi-modal vasopressor therapy is relevant as we move to a more precision medicine-based approach to management of septic shock. [16,17]

Angiotensin II has been seen to improve hemodynamics and decrease background vasopressor use in a phase III trial published in 2017.[13] Since then significant new evidence using real world and post hoc data has supported survival benefit in a cohort of patients with septic AKI,[43] appropriately resuscitated patients already on vasopressin,[44] those with serum renin greater than population median,[12] and also for responders to very low dose Angiotensin-II.[45] While the phase III trial reported no difference in serious adverse events attributable to vascular thromboses, the authors did report an overall difference in all vascular events that did not favor Angiotensin II.[13,46] This has not been seen in real world utilization studies reported so far.[47]

Lastly, the use of stress dose corticosteroids is recommended in patients who require ongoing vasopressor infusion to maintain MAP greater than 65 mmHg. Hydrocortisone 200 mg/day dosed 50 mg every 6 hours is a typical regimen and has been shown to increase vasopressor-free days.[48]

Anaphylactic Shock

Epidemiology and Pathophysiology

Anaphylaxis and anaphylactoid reactions produce rapid multisystem organ failure through mast cell activation. Fatal anaphylaxis is quite rare with less than one death in one million report in the United States, however the overall incidence is around 5%.[49] Symptoms relate to mast cell degranulation and the release of histamine, tryptase, heparin, tumor necrosis factor, and other inflammatory mediators. Clinical signs include rash, bronchorrhea, bronchospasm, status asthmaticus, swelling, low venous tone and massive fluid extravasation resulting in low preload, tachycardia and depressed myocardial function.[50] A diagnosis of anaphylaxis is made when the

following criteria are met: a rapid and sudden progression of symptoms involving skin and/or mucosa, as well as life-threatening airway, breathing, or circulation problems. [51]An elevated blood serum tryptase greater than 1.2x baseline sent within the first hour of exposure is considered confirmatory though use of this laboratory result is imperfect. The need for improved biomarkers of anaphylaxis exists.[52] Symptoms typically peak quickly, but may present with a biphasic pattern hours or days after exposure to the offending agent, and vary rarely symptoms may linger for days or weeks. The degree of resultant shock may be profound and its course difficult to predict. Tissue hypoxemia and ischemia may result in end-organ damage despite maximal pharmacologic support. Stress-induced cardiomyopathy has been described in several case reports as has coronary vasospasm.[53,54]

Monitoring

Rapid recognition and treatment require cessation of the offending agent and first and foremost intramuscular epinephrine (by injection into the mid-lateral thigh, 0.01 mg/kg of a 1:1000 (1 mg/mL) solution to a maximum of 0.5 mg in adults and 0.3 mg in children), as delay in epinephrine administration can increase risk of mortality. A second dose of epinephrine may be administered to adults and children with severe anaphylaxis whose symptoms are not relieved by an initial dose. Intravenous epinephrine may be dosed instead of intramuscular as 50 micrograms at a time for adults and 1 microgram/kg for children.[55] High-volume fluid administration may be required. Oxygen should be administered, and the airway should be secured as quickly as possible if needed. Steroids and antihistamines address mast cell degranulation but are not first line therapy. Bronchodilators may be used to treat bronchospasm. In severe reactions, epinephrine infusion as well as vasoconstrictors should be added for continued support of cardiac output and perfusion pressure. In rare cases the use of mechanical

circulatory support to optimize tissue perfusion is needed using intra-aortic balloon pump, VV-ECMO, and VA-ECMO.[56]

Neurogenic Shock

Epidemiology and Pathophysiology

Neurogenic shock, the subset of physiologic effects resulting from spinal shock, usually results from traumatic spinal cord injury. It can present within minutes and last for weeks after spinal cord injury. Neurogenic shock carries an incidence of approximately 30% in cervical spinal cord injury. This entity is characterized by hypotension due to loss of spinal cord reflexes below the level of the injury and a loss of sympathetic tone.[57] It is caused by loss of descending sympathetic pathways resulting in predominant parasympathetic tone, leading to reduced venous return, bradycardia, and decreased vascular resistance.[58]

Monitoring

Patients with neurogenic shock should be monitored in an ICU with continuous blood pressure measurements, telemetry and pulse oximetry. These patients have a high incidence of respiratory failure, particularly in mid-thoracic SCI and above.[59] Patients with thoracic SCI and above have a higher incidence of severe bradycardia and bradyarrhythmia.[22]

Management

Early surgical stabilization is key to treating and stabilizing spinal cord injury and resultant neurogenic shock. Despite a paucity of evidence, maintaining mean arterial pressure of 80-90/ mmHg with the use of vasoconstrictors is recommended to augment spinal cord perfusion pressure.[60] The use of appropriate agent here may be determined by factors such as high spinal injury where preference would be for additional inotropy via norepinephrine while in other situations phenylephrine with unopposed alpha agonism may be appropriate. However,

functional outcomes suggest that if a spinal cord injury and resultant neurogenic shock are profound enough, the use of vasoconstrictors does not confer improved functional status despite increasing spinal cord perfusion pressure.[61] High dose methylprednisolone has been used for the treatment of neurogenic shock but the evidence in favor is scarce and the infectious complications profound.[62] Overall, supportive care is recommended to maintain end-organ perfusion and an appropriate heart rate.

**Cardiogenic Shock**

Epidemiology and pathophysiology

Cardiogenic shock is a low output state due to primary cardiac dysfunction leading to systemic decompensation, end organ dysfunction, and secondary myocardial injury. Known cardiac dysfunction with systolic blood pressure < 80-90 mmHg, a cardiac index < 1.8 L/min/$m^2$ without support and < 2.2 L/min/$m^2$ with support, and signs of tissue hypoperfusion are hallmarks of cardiogenic shock.[63-67] Despite advances in care, mortality remains high and to the tune of 40-67%.[68] The Society of Cardiovascular Angiography and Interventions (SCAI) has developed a tiered classification system to standardize the definition and severity of cardiogenic shock to allow for more timely risk stratification and interventions and ultimately improved outcomes. (Table 2)[69]

The most common cause of cardiogenic shock is acute coronary syndrome (ACS) and resultant LV dysfunction, which accounts for up to 81% of cardiogenic shock patients, followed by acute decompensated heart failure. (Table 3)[67,70] Hemodynamic phenotypes reflect the effects of cardiogenic shock on cardiac function and systemic vascular resistance (SVR) and end organ perfusion. "Cold and wet" is the classically described presentation of cardiogenic shock and denotes the presence of cool extremities and pulmonary congestion due to left ventricular failure

and compensatory peripheral vasoconstriction, often poorly tolerated by a struggling pump.[66] "Cold and dry" CS, as the term suggests, correlates with poor systemic perfusion in the absence of pulmonary congestion and is often responsive to diuretic therapy. The systemic inflammatory response that occurs in cardiogenic shock is often underappreciated and is described as "wet and warm," where peripheral vasodilation predominates. Cor pulmonale, isolated right ventricular (RV) failure, is beyond the scope of this review, but the presence and degree of RV and LV failure also affects the clinical presentation of CS. These are important to identify early on, as these parameters determine management strategies (e.g., type of inotropic support, afterload reduction, diuretic use, etc.).

Diagnosis

Serial troponins and electrocardiogram (ECG) are essential investigations in cardiogenic shock to identify acute coronary syndrome (ACS) and myocardial necrosis.[67] If evidence of ST elevation Myocardial Infarction (STEMI) or other changes concerning ACS are noted, emergent coronary angiography and determinations of revascularization needs are warranted. Conversely ST and non-ST abnormalities can also signify myocarditis, decompensated heart failure, or other structural disorders that cause CS.[66,71] Elevations in cardiac biomarkers BNP and NT-proBNP are seen in patients with LV and RV dysfunction but it is important to note that elevations are seen in all shock states and are linked to worse outcomes, regardless of the type of shock. As such, it is not recommended to utilize BNP or pro-BNP to assess treatment response in cardiogenic shock. [72] Lactate elevations are independently associated with increased mortality in cardiogenic shock and frequent monitoring to assess response to therapies is recommended.[67] Reuda et al analyzed identified 4 key proteins (liver-type fatty acid-binding protein, beta-2-microglobulin, fructose-bisphosphate aldolase B, and SerpinG1) that combined (CSP4) had

significant predictive value for short-term mortality in cardiogenic shock when used in conjunction with contemporary risk scoring tools. [73]This may guide shock teams in targeted care for patients with cardiogenic shock and warrants further study.

In addition to standard ICU monitoring and arterial pressure monitoring, PAC should be strongly considered as clinical presentations often correlate and drive decision making in the management of cardiogenic shock. Thermodilution cardiac output is readily obtained and values measured assist in the calculation of cardiac power output, cardiac power index (CPI) and pulmonary artery pulsatility index (PAPI). Mixed oxygen saturation ($SvO_2$) is reduced in cardiogenic shock but can also reflect anemia, hypoxemia, or increased oxygen consumption.

Echocardiography will provide ejection fraction (EF) and degree of biventricular dysfunction and will detect structural and valvular issues contributing to cardiogenic shock and to confirm placement of mechanical circulatory support (MCS) devices.[67] In addition to rapid detection of gross functional abnormalities, point of care ultrasound (POCUS) can be useful in ruling out common alternative diagnoses eg, cardiac tamponade or pneumothorax. The presence of three or more B-lines in at least 2 regions of the lung bilaterally on POCUS in the presence of lung sliding points toward pulmonary congestion due to cardiogenic acute pulmonary edema. [74]

Management

The goals of management are to restore perfusion to the myocardium and end organs while treating the underlying cause of failure. If ACS is present based on data available early invasive treatment and reperfusion is the mainstay of treatment. Importantly, emergent revascularization compared to medical therapy in patients with cardiogenic shock has shown mortality benefits across multiple racial and ethnic subgroups.[67,75]

In general, best practices propose that cardiac index should be kept above 2.2 L/min/$m^2$ and MAP goals > 65 mmHg. However, further studies are needed to determine ideal goals in CS. While the use of right atrial pressures and pulmonary artery wedge pressures are poor predictors of fluid response, overall trends along with correlation with echocardiographic findings, physical exam, and biochemical markers may be useful.

While catecholamines may transiently improve hemodynamics, they are associated with worse long-term outcomes in patients with heart failure with reduced ejection fraction (HFrEF),[76] potentially due to their arrhythmogenicity and increased myocardial oxygen consumption. A recent randomized control trial looking at the use of dobutamine versus milrinone in cardiogenic shock found no difference in outcomes.[77] Thus, benefits of a catecholamine sparing agent in this setting should be weighed against the need for rapid titration and possibility of concomitant renal failure in shock. While sinus tachycardia is often a compensatory mechanism seen in cardiogenic shock due to HFrEF, new onset tachyarrhythmias (e.g., atrial fibrillation) may require urgent cardioversion. Lastly, negative inotropes (e.g., beta-blockers) should be avoided in cardiogenic shock and consideration of chemical or electrical pacing is warranted if brady-arrhythmias are contributing to hypoperfusion.

If indicated, judicious challenges of 250 to 500 ml are recommended to avoid overstressing the failing pump. Conversely, fluid removal with furosemide and/or the addition of a thiazide diuretic should be considered if increased congestion and overall total body volume is elevated.

Respiratory failure occurs when cardiogenic pulmonary edema impairs gas exchange and worsens shunt. Because venous return is reduced both to the left and right ventricles with positive pressure ventilation (PPV), the overall effect on cardiac output is variable and dependent

on other factors which include preload, afterload, severity of left and right ventricular dysfunction and degree of interventricular interdependence. Positive pressure ventilation can improve oxygenation and thereby decrease RV afterload by decreasing hypoxic pulmonary vasoconstriction as well as LV afterload. Non-invasive PPV is often used initially when respiratory insufficiency presents in cardiogenic shock and may decrease likelihood of endotracheal intubation. However, intubation is often unavoidable, especially if it is compounded by the presence of chronic respiratory co-morbidities and other acute issues such as aspiration, altered mental status risk, facial trauma or deformities, severe hemodynamic instability or recent GI or upper airway surgery where non-invasive positive pressure ventilation is contraindicated. [78] Moderate to high PEEP (5-15cmH20) may improve overall CO and end organ perfusion in afterload dependent LV failure. [79] Low tidal volume (4-6 ml/kg) is lung protective, and daily assessments to minimize sedation and increase mobility are important in this setting.[78]

While beyond the scope of this review, if hemodynamic support is inadequate despite maximal medical management, temporary MCS should be considered. Cannulation strategies, physiologic effects and amount of support vary based on the type of MCS initiated. Early initiation of MCS may confer survival benefit.[80] Given the high mortality in cardiogenic shock and the risks and substantial costs associated initiation of temporary MCS, shock algorithms and multidisciplinary expertise at regional hubs are particularly useful as they allow for early involvement of clinical experts and time-sensitive, patient-centered decision making on appropriate treatment and support strategies.[59] If no recovery is observed on MCS, temporary MCS can serve as a bridge to advanced therapies with transplantation or durable support devices or bridge to decision as further workup is obtained. Neurologic uncertainty or multisystem organ failure prohibit advanced therapies candidacy, goals of care discussions should occur, and

consideration of withdrawal of support should be initiated if there is poor chance of recovery without exit strategy on MCS.

**Obstructive Shock**

Epidemiology and Pathophysiology

Obstructive shock is caused by a physical impediment of blood flow in the cardiovascular system.[81] It is the least common type of shock, constituting about 2% of all shock states.[82] Tension pneumothorax (TP), cardiac tamponade , and pulmonary embolism (PE) comprise the majority of obstructive shock cases, but any obstruction that restricts venous return, prevents diastolic filling, or severely elevates afterload can result in obstructive shock.[82-84] Grouping based on location, mechanism, or cardiac consequences has been used[81,85-87] with categorization centered around effects on ventricular preload and afterload being most intuitive for an anesthesiologist. (Table 4)

Diagnosis and Management

Patient presentation varies depending on etiology, acuity, and severity.[81,85-87] Initially, symptoms may be nonspecific, such as shortness of breath or chest pain. Additionally, initial physiologic perturbations may be limited to compensatory responses like tachycardia and tachypnea. Physical exam frequently reveals jugular venous distention, abnormal auscultatory findings, and cool extremities.[81,85-87] As the obstruction progresses, hemodynamic indices resemble low-output states, with laboratory values consistent with oxygen supply and demand mismatch. Intravascular volume and cardiac contractility are usually preserved; however, cardiac output (CO), stroke volume (SV), and mean arterial pressure are decreased.[81,85-87] Finally, systemic vascular resistance and central venous pressure (CVP) are usually increased, while wedge pressure varies based on etiology. For patients in extremis, diagnosis is clinical in nature,

and treatment should not be delayed for diagnostics. Therapies most often consist of pharmacotherapy followed in quick succession with percutaneous or surgical relief of the obstruction.[81,85-87]

Tension Pneumothorax

Epidemiology and Pathophysiology

Development of tension pneumothorax is uncommon with poorly quantified incidence.[88,89] Most commonly, it is observed in trauma, ARDS, and mechanically ventilated populations, but a simple pneumothorax can convert to tension physiology if one-way valve communication exists between the alveolus and pleura. Tension pneumothorax occurs when trapped air accumulates in the pleural space, increasing intrapleural pressure above the atmospheric pressure, leading to ipsilateral lung collapse and mediastinal compression with contralateral shift.[88]

Diagnosis and Management

Cyanosis, tracheal deviation, decreased breath sounds, percussion hyperresonance, and subcutaneous emphysema point towards the diagnosis of TP.[88] As TP evolves, compensatory mechanisms are frequently successful in maintaining stability in spontaneously breathing patients.[6,90] Conversely, pneumothorax developed during mechanical ventilation progresses to hemodynamic instability up to 70% of cases.[88-90] Elevated peak and plateau airway pressures, with decreasing lung compliance may be observed. Utilization point-of-care ultrasonography (POCUS) may facilitate faster diagnosis of a pneumothorax, with higher sensitivity than a chest radiography (79% vs 40%) and similar specificity (98% vs 99%).[91] POCUS findings suggestive of pneumothorax include lack of lung sliding and lung pulse, presence of lung point, and barcode sign on motion mode (M-mode).[92] Nonetheless, TP is a clinical diagnosis and treatment should

not be delayed to obtain imaging. Therapy consists of emergent placement of large-bore needle into the anterior second intercostal space in the midclavicular line, followed by a percutaneous, small-bore thoracostomy catheter.[93,94]

## Cardiac Tamponade

### Epidemiology and Pathophysiology

Cardiac tamponade is a feared consequence of any pericardial content accumulation, including blood, clot, pus, chyle, and gas.[95-98] It is characterized by restriction of cardiac filling due to elevation of intrapericardial pressure. Initial compensatory responses include elevation of systemic and pulmonary venous pressures, and tachycardia. As left and right ventricular diastolic, right atrial, and wedge pressures equalize, early diastolic filling (Y-descent) fades and ventricular filling (X-descent) becomes predominant. With progression, pulsus paradoxus results due to ventricular interdependence.[95,97]

### Diagnosis and Management

Diagnosis of cardiac tamponade is also clinical in nature, but echocardiography is used in most instances.[95,97] Classically, physical exam may reveal muffled heart tones, jugular venous distention, and systolic inspiratory variation of greater than 10 mmHg, but these may be difficult to appreciate in a perioperative setting.[95,97] Microvoltage and electrical alternans may be seen on ECG with large effusions.[95,97] Pulsus paradoxus maybe still be observed on an arterial line tracing by monitoring inspiratory and expiratory area under the curve. High value occurring on inspiration and low on expiration in mechanically ventilated patients has been previously coined as reversed pulsus paradoxus but is nothing different than what is commonly described by anesthesiologists as pulse pressure variation.[99,100] Echocardiographic imaging shows diastolic collapse of the right ventricle (highly specific), systolic collapse of the right atrium (early sign),

plethoric IVC with hepatic flow reversal, and respiratory variation of mitral and/or tricuspid valve inflow velocities have been classically associated with tamponade physiology.[101]

Recognizing cardiac tamponade after cardiac surgery is especially problematic and requires a high degree of suspicion.[102] Because the pericardial sac is often left open and in communication with pleural spaces preventing large fluid collections, it is usually a localized pocket of clot pressing on one cardiac chamber that causes cardiac tamponade. In effect, an insidious presentation ensues. Gradually worsening hypotension, low cardiac output, increasing filling pressures, and increasing inotropic and pressor support are encountered. Worsening lactic acidosis is also observed, but classic equalization of pressures usually does not occur.[102] To aid in diagnosis, transesophageal echocardiography (TEE) is frequently utilized with success, but its limitations should be understood, as it may be insufficient to find regional clots, appreciate tissue edema, or illustrate chamber collapse when contaminant cardiac pathology is present.[102]

Treatment requires evacuation of the pressurized pericardial content. This can be achieved with percutaneous or surgical techniques.[95,97] While awaiting definitive treatment, patients should be temporized with enhancement of venous return with volume administration or leg elevation, promotion of chronotropy/inotropy and systemic venous pressure with epinephrine boluses, and reduction of intrathoracic pressure by limiting tidal volume and positive end expiratory pressure (PEEP).[102]

Pulmonary Embolism

Epidemiology and Pathophysiology

PE may result in obstructive shock when two or more lobar arteries and at least 50-60% of vascular bed are affected, elevating pulmonary vascular resistance.[81] Resultant acute elevation of right ventricular (RV) afterload leads to chamber enlargement and myocardial failure. In

effect, a decrease in early diastolic filling and preload of the LV leads to reduction in SV and CO.[81,85]

Diagnosis and Management

Patient presentation varies with severity. Patients with altered mental status, hypotension, elevated cardiac troponins, and BNP are at increased risk of mortality and adverse outcomes.[103,104] Use of tools like Pulmonary Embolism Severity Index (PESI), or simplified PESI (sPESI) is encouraged as they can aid in risk stratification and therapy selection.[104]

Although computed tomography pulmonary angiography is a diagnostic gold standard, POCUS may be used as a bedside tool to rule-in a diagnosis of a PE. POCUS has a high specificity and low sensitivity for the diagnosis, and relies on indirect evidence like RV failure or deep venous thrombosis.[105] RV dysfunction on POCUS can be recognized by evaluating tricuspid annular plane systolic excursion (TAPSE), lateral tricuspid annular systolic velocity (S'), or short pulmonary flow acceleration and low tricuspid regurgitant pressure gradient (60/60 sign).[106] Pressure overload of the RV can be recognized by septal flattening in systole. The size of the RV can be qualitatively estimated by comparison to the neighboring LV.[105] Free wall akinesis with apical sparing (McConnell's sign) is frequently associated with a diagnosis of a PE, but its specificity lies in recognition of acute right heart strain, regardless of the cause.[106,107] Rarely, thrombus-in-transit may be observed and is the only pathognomonic ultrasonographic finding indicative of an acute PE in a symptomatic patient.[108]

PE with hypotension (massive PE) is the most severe type, where hypotension is defined as SBP < 90 mmHg for > 15 minutes.[109] Patients with hypotension, shock, myocardial dysfunction, and low risk of bleeding should undergo systemic thrombolytic therapy.[109] Catheter-based thrombus removal may be an option in patients with high risk for bleeding or

failed systemic thrombolysis.[109] Surgical embolectomy may also be of benefit.[110] Given that therapies frequently depend on local expertise, standardization of in-hospital care is now recommended. Development of Pulmonary Embolism Response Teams (PERT) helps to improve quality, efficiency, and multidisciplinary communication, resulting in improved outcomes.[111,112]

**Hypovolemic Shock**

Hypovolemic shock is from a loss of intravascular volume, either directly from the loss of whole blood or indirectly from extracellular volume loss, that leads to inadequate organ perfusion[8,86,113] Ultimately, all types of hypovolemic shock decreases preload, which leads to a deficit in perfusion pressure and consequently, macrocirculation and microcirculation suffer. The resulting poor circulation results in decreased tissue perfusion and triggering of an inflammatory cascade.[86] External fluid losses include insensible losses (e.g., open surgical abdominal procedures or hyperthermia). Internal fluid losses include gastrointestinal causes (e.g., prolonged *nil per os* (NPO) times, persistent vomiting, or diarrhea) and renal causes (e.g., diabetes insipidus (DI), polyuric phase of acute tubular necrosis recovery).[86] Hypovolemic shock that is due to the loss of whole blood is termed hemorrhagic shock, and when associated with soft tissue injury is termed traumatic hemorrhagic shock. Traumatic hemorrhagic shock is more common than non-traumatic causes of blood loss.[86,113] Hemorrhagic shock includes perioperative hemorrhage (e.g., postoperative bleeding), gastrointestinal hemorrhage (e.g., varices, ulcers), maternal hemorrhage (e.g., uterine atony, placental abruption), and vascular rupture (e.g., aneurysm).[86,114] Traumatic hemorrhagic shock includes soft tissue injury in addition to active hemorrhage. This distinction is important because the presence of soft tissue injury has additional implications on the effects of shock.[115] For instance, available evidence shows that soft tissue injury increases likelihood of

disruption of the blood-endothelium interactions, may accelerate coagulopathy through mechanisms that exacerbate tissue hypoxia.[115]

Epidemiology and Pathophysiology

The pathophysiology of hypovolemic shock that is due to the loss of extracellular fluid varies according to the underlying cause. However, in all these cases daily fluid loss exceeds daily intake. The primary method of water intake is through the consumption of fluids and food, and the primary method of water loss is through urine, sweat, and stool. Fluid loss that is easily quantified is termed sensible loss, such as urine output. Fluid loss that is not easily measured is termed insensible loss, and is estimated to reach up to 800 ml/day. Insensible fluid loss largely occurs through water excretion in the stool, skin, and respiratory system.[116] Prolonged NPO times contribute to hypovolemia by decreasing intake in the context of continued sensible and insensible fluid loss.

Profound sensible losses can also lead to hypovolemic shock, as is seen with DI. DI is a condition where there is either a defect in the production or utilization of Antidiuretic Hormone (ADH), the key posterior pituitary polypeptide that is responsible for the conservation of fluid at the distal convoluted tubule. In central DI, there is a deficiency of ADH. In nephrogenic DI, ADH levels are normal; however, the kidney is unable to respond to the hormone. In both types of DI, patients release large volumes of dilute urine. If untreated, these patients are at risk for hypovolemic shock.[117]

Hemorrhagic Shock and Traumatic Hemorrhagic Shock

The pathophysiology of hemorrhagic and traumatic hemorrhagic shock has been under study for many years, and the effects are far reaching on the tissue level, vascular level, and cellular level. On the tissue level, hemorrhage leads to hypovolemia, which in turn leads to reflex

vasoconstriction. This vasoconstriction leads to decreased blood flow to vital organs and consequent multisystem organ failure in severe cases.[114] Hemorrhage also affects the vascular endothelium in both a local and generalized fashion.[115] Locally, thrombus formation is promoted through platelet activation, and the consequent formation of a platelet thrombin plug and the site of injury.[118] However systemically, the glycocalyx is shed due to the increased catecholamines and oxygen debt.[119] Glycocalyx shedding can lead to increased fibrinolytic activity and auto-heparinization, which lead to coagulopathy.[115] Of note, glycocalyx shedding combined with leukocyte endothelial interactions also results in capillary leak syndrome.[86] Coagulopathy is compounded by decreased platelet numbers as well as decreased platelet activity.[114] The soft tissue injury in traumatic hemorrhagic shock contributes to and likely accelerates coagulopathy, possibly through mechanisms that worsen tissue hypoxia.[115] The hypothermia and acidosis found in trauma patients also exacerbate active bleeding.[86]

Effects are also complex at the cellular level. In both hemorrhagic and traumatic hemorrhagic shock, the acute reduction of red blood cell quantity causes inadequate oxygen delivery to cells, thereby forcing transition to anaerobic metabolism.[115,120] Byproducts and wastes including lactic acid, inorganic phosphates and oxygen radicals begin to accumulate leading to acidosis. As cellular metabolism begins to fail, dying cells release damage-associated molecular patterns (DAMPs, alarmins and other intracellular molecules) that activate the innate immune system thereby triggering a systemic inflammatory response.[121]

Diagnosis and Management

Elevated lactate and base deficit are a characteristic finding in hemorrhagic shock. However, acid-base balance ultimately depends on the underlying cause of the hypovolemic shock. For example, gastrointestinal losses can result in metabolic alkalosis, such as in the case

of persistent vomiting. In hemorrhagic shock hemoglobin and hematocrit are usually severely decreased. However, if hemoconcentration is present, these values will be increased.[115]

Pulse pressure variation (PPV) in appropriately ventilated patients in sinus rhythm is regarded as a useful measure of volume responsiveness. PPV reliability can be compromised by elevated respiratory rates, right ventricular failure, and decreased chest wall compliance. Trends in CVP monitoring over time are also frequently used to assess intravascular volume status. CVP values should be interpreted in the context of ventilator settings and can be compromised by patient chest wall compliance and right ventricular function as well. With the current ubiquity of ultrasound, measurement of the inferior vena cava throughout the respiratory cycle has also become another indicator for intravascular volume status.[115]

Laboratory studies frequently reveal evidence of pre-renal kidney injury: elevated blood urea nitrogen, serum creatinine, and urine osmolality; reduced urine sodium with fractional excretion of sodium less than 1%; and high or low serum sodium and potassium depending on the underlying cause.[115] In hemorrhagic shock, platelet counts can be decreased mainly due to dilutional effects and hemoglobin and hematocrit will be low unless hemoconcentration is present., INR, PT, and aPTT can be elevated and fibrinogen levels can be decreased.[122] Thromboelastography is an excellent tool for the monitoring of clot formation and can help guide transfusion decision-making.

The “Stop the Bleed” concept of successful treatment of hypovolemic shock ultimately depends on the definitive correction of the underlying cause, and on the ability to temporize the patient with balanced resuscitation and vasopressors in the interim. To help temporize initial bleeding, the American College of Surgeons began the STOP THE BLEED campaign. The purpose of the initiative is to educate the public on hemorrhage control tactics following

manmade or natural disasters.[123] The program improved the confidence and willingness of laypersons to render aid, and showed increased tourniquet use following program rollout.[124]

En route to the hospital, it is preferable to avoid aggressive resuscitation with crystalloid solutions in order to avoid clotting factor dilution, hemodilution and the consequent exacerbation of hypoxia.[114] If fluid administration alone is insufficient to restore adequate perfusion (SBP <80 mmHg), it may be necessary to temporize blood pressure with vasopressors. While there remains controversy regarding the optimal time to initiate vasopressors as well as choice of agent, norepinephrine has been suggested as first line.[125] This due to its sympathomimetic properties as well the potential benefit of splanchnic venoconstriction and movement of blood volume to the central circulation thereby increasing venous return and cardiac output. Importantly phenylephrine, often used in clinical practice may have opposing effects on the splanchnic pre-portal and hepatic veins, thereby decreasing venous return and consequent downstream effects. In the hospital, definitive bleeding control is priority as well as adequate restoration of euvolemia via balanced resuscitation. Blood products are transfused in ratios that resemble whole blood, usually at a 1:1:1 ratio of packed red blood cells, fresh frozen plasma, and platelets. Massive transfusion protocols initiated at this rate improve morbidity and mortality of trauma patients in hemorrhagic shock.[126]

**Conclusions**

Shock is a common and often life-threatening problem in the critically ill. Early diagnosis and intervention are a cornerstone for all flavors of this pathophysiological state. Multimodal therapeutics, new diagnostic tools and consistent evidence-based protocolized practices have been shown to improve outcomes. A single patient may transition from one shock state to

another, therefore a vigilant approach that involves close and repeated re-evaluation is always a necessity. Future work is needed to fill current gaps in available guidelines for management of shock, such as clear recommendations for non-septic vasodilatory shock, timing of initiation of vasopressors in relationship to fluids and adjuvants, and management of shock in patients with right ventricular failure or those on mechanical circulatory support.[14,38] Appropriate resuscitation goals continue to evolve as we explore the interplay between microcirculatory and macrocirculatory dysfunction and the role of optimal blood pressure, flow dynamics, and peripheral perfusion as therapeutic targets.[127]

Table 1: Basic diagnostic and management elements of shock states

| Shock State | SVR | HR | CO | CVP/ Preload | $ScvO_2$ | Exam/Findings‡ | Treatment |
|---|---|---|---|---|---|---|---|
| **Distributive** | ↓ | ↑ | Varies† | ↓ | ↑ | Septic: Febrile, leukocytosis, possible focal infection<br><br>Anaphylaxis: rapid onset, urticaria, hives, febrile, swelling, bronchospasm<br><br>Neurogenic shock: spinal cord injury, loss of sensation and motor tone, altered reflexes | Septic: Empiric antibiotic, fluids, vasoconstrictors, source control<br><br>Anaphylaxis: stop culprit, epinephrine, steroids, fluids<br><br>Neurogenic shock: surgical stabilization, BP augmentation |
| **Cardiogenic** | ↑ | ↑ | ↓ | ↑ | ↓ | Cold extremities, rales, elevated JVD, slow capillary refill | Inotropic support; pacing if bradycardic; treat arrythmia; mechanical support if indicated |
| **Obstructive** | ↑ | ↑ | ↓ | ↑ | ↓ | Elevated JVD, tachycardic, distant heart sounds, pulsus paradoxus, electrical alternans | Decompress tension pneumothorax; pericardiocentesis; pulmonary thrombectomy |
| **Hypovolemic** | ↑ | ↑ | ↓ | ↓ | ↓ | Hemorrhage, possible insensible losses, low JVD, dry mucus membranes | Hemorrhage control if applicable; fluid resuscitation |

SVR: systemic vascular resistance; HR: heart rate; CO: cardiac output; CVP: central venous pressure; $ScvO_2$: central venous oxygen saturation; JVD: jugular venous distension; BP: blood pressure

†**Early septic shock**, usually increased; **late septic shock** with low preload, may be decreased despite hyperdynamic state; **septic cardiomyopathy**, will be decreased; **anaphylactic shock**: usually increased hyperdynamic unless stress-induced cardiac dysfunction; **neurogenic shock**: depends on level of injury and whether sympathetic cardiac accelerators involved.

‡All shock states will have overlap of: low urine output, altered mental status

Table 2. SCAI Classification of Cardiogenic Shock (CS)

| CS Stage | Physical Examination | Biochemical markers | Hemodynamics | |
|---|---|---|---|---|
| A. At Risk | Normal CVP, no rales, warm, good peripheral pulses, normal mentation | Normal labs, lactate and renal function | SBP > 100 or normal for patient. If done: CI $\geq$ 2.5, CVP < 10, $S_vO_2 \geq 65\%$ | At risk for CS: large acute MI or prior infarct, worsening heart failure symptoms |
| B. Beginning CS | Increased CVP, good peripheral pulses, normal mentation | Minimal renal functional impairment, elevated BNP | SBP < 90 or MAP < 60 or > 30 decrease, HR $\geq$ 100. If done: CI $\geq$ 2.2, $S_vO_2 \geq$ 65% | Clinical evidence of hypotension or tachycardia without hypoperfusion |
| C. Classic CS | May include any: Looks unwell, panicked, ashen, volume overload, rales, Killip class 3-4, cold/clammy, altered MS, decreased UO | May include any: Lactate > 2, doubling creatinine or 50% drop in GFR, increased LFT's or elevated BNP | May include any: SBP > 90, MAP <60 or >30 decrease, and drugs/device used to maintain BP above target, CI < 2.2, $P_{pao} \geq$ 15, CVP/$P_{pao} \geq$ 0.8, PAPI < 1.85, CPO $\leq$ 0.6 | Clinical signs of hypoperfusion that requires intervention pharmacologically or with temporary MCS, typically with hypotension |
| D.Deteriorating/ Doom | Any of Stage C and deteriorating | Any of Stage C with progressive worsening | Any of Stage C and require multiple pressors and/or mechanical circulatory support to maintain flow | Not responding to initial interventions in Stage C |
| E. Extremis | No SBP without resuscitation or maximal support to sustain ROSC, PEA or refractory VT/VT | "Trying to die," pH $\leq$ 7.2, lactate $\geq$ 5 | SBP without resuscitation, pulseless electrical activity, refractory VT/VF, hypotension despite maximal support | Near pulselessness and/or cardiac collapse or CPR, with or without initiation of ECMO, mechanical ventilation, |

| | | | | |
|---|---|---|---|---|
| | | | | pacing, etc |

BNP, brain natriuretic peptide; CI, cardiac index; CPO, cardiac power output; CS, cardiogenic shock; CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; GFR, glomerular filtration rate; LFTs, liver function tests; MAP, mean arterial pressure; MCS, mechanical circulatory support; MI, myocardial infarction; MS, mental status; PAPI, pulmonary artery pulsatility index; $P_{pao}$, pulmonary artery occlusion pressure;SBP, systolic blood pressure; SCAI, Society for Cardiovascular Angiography and Intervention, $S_vO_2$, mixed venous $O_2$ saturation; UO urine output; VT/VF, ventricular tachycardia/fibrillation.

Modified from Baran, *et al.*[69,128]

Table 3. Etiologies of Cardiogenic Shock

I. Ischemic:
    a. Acute myocardial infarction secondary to LV or RV infarct
    b. Mechanical complication of ischemic infarct
II. Nonischemic
    a. Acute on chronic decompensated heart failure
    b. Acute decompensated heart failure
        i. Chronic ischemia
        ii. Dilated cardiomyopathy
        iii. Myocarditis
        iv. Stress induced cardiomyopathy (Takutsubo)
        v. Pregnancy associated heart disease
            1. Peripartum cardiomyopathy
            2. Coronary artery disease
    c. Post cardiotomy cardiogenic shock
    d. Post cardiac arrest myocardial stunning
    e. Septic cardiomyopathy
    f. Myocardial Contusion
    g. Dynamic LVOT obstruction
        i. Hypertrophic obstructive cardiomyopathy
        ii. Hypertensive cardiomyopathy
        iii. Takutsubo

RV, right ventricular; LV, left ventricular; LVOT, left ventricular outflow tract.

Adapted from Van Diepen *et al.*[67,129]

Table 4. Etiologies of Obstructive Shock

| **IMPAIRED PRELOAD/DIASTOLIC FILLING** |
|---|
| Mediastinal Tumors[130] |
| SVC Syndrome[131] |
| Tension Pneumo/hemothorax |
| Right Sided Cardiac Herniation – vascular torsion[132] |
| Left Sided Cardiac Herniation – LV compression/compromise[132] |
| Cardiac Tamponade |
| Constrictive Pericarditis[81] |
| Cardiac Tumors[133] |
| Severe Pulmonary Hypertension – effect on the LV[81] |
| Massive PE – effect on the LV |
| High Grade Abdominal Compartment Syndrome – effect on venous return[134] |
| Auto-PEEP/Excessive Intrathoracic Pressure[85] |
| Giant Hiatal Hernia[83] |
| **ELEVATED AFTERLOAD** |
| Massive PE – effect on the RV |
| Severe Pulmonary Hypertension – effect on the RV |
| Aortic Occlusion[84] |
| Coarctation of the Aorta[135] |
| High Grade Abdominal Compartment Syndrome – effect on the LV[134] |

Legend: LV = left ventricle, PE = pulmonary embolism, PEEP = positive end-expiratory pressure, RV = right ventricle

Table 5. Etiologies of Hypovolemic Shock

| **EXTRACELLULAR FLUID LOSS** |
|---|
| **External Losses – Insensible Losses** |
| Open abdominal procedures |
| Hyperthermia |
| Respiratory System |
| **Internal Losses – Gastrointestinal or Renal** |
| Prolonged NPO times |
| Persistent vomiting |
| Persistent diarrhea |
| Diabetes Insipidus |
| Polyuric phase of acute tubular necrosis recovery |
| **LOSS OF WHOLE BLOOD** |
| **Hemorrhagic Shock – Perioperative, Gastrointestinal, Maternal or Vascular Rupture** |
| Postoperative bleeding |
| Esophageal Varices |
| Gastrointestinal Ulcers |
| Uterine atony |
| Placental abruption |
| Aneurysmal rupture |
| **Traumatic Hemorrhagic Shock** |
| Includes the presence of soft tissue injury in addition to active hemorrhage, e.g. motor vehicle collision |

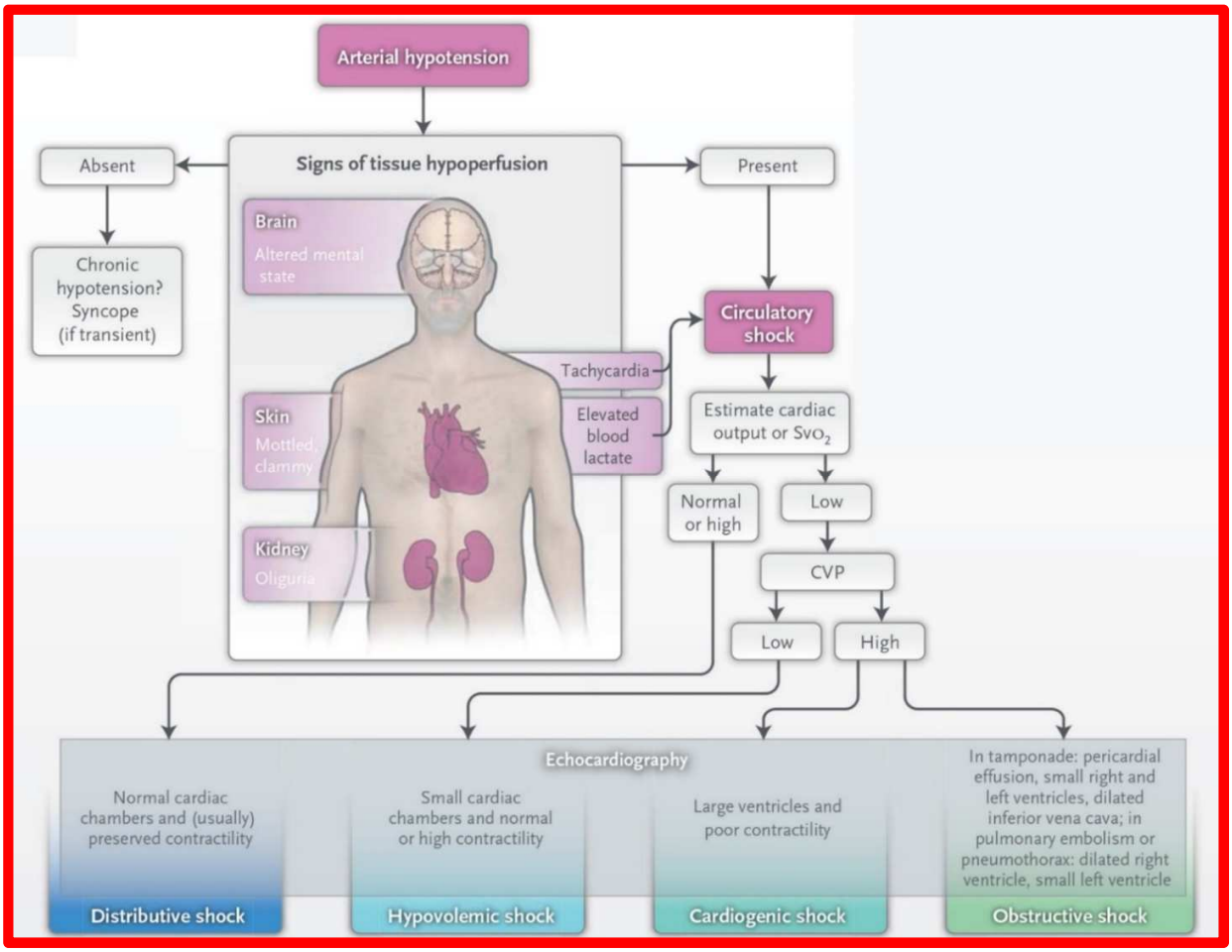
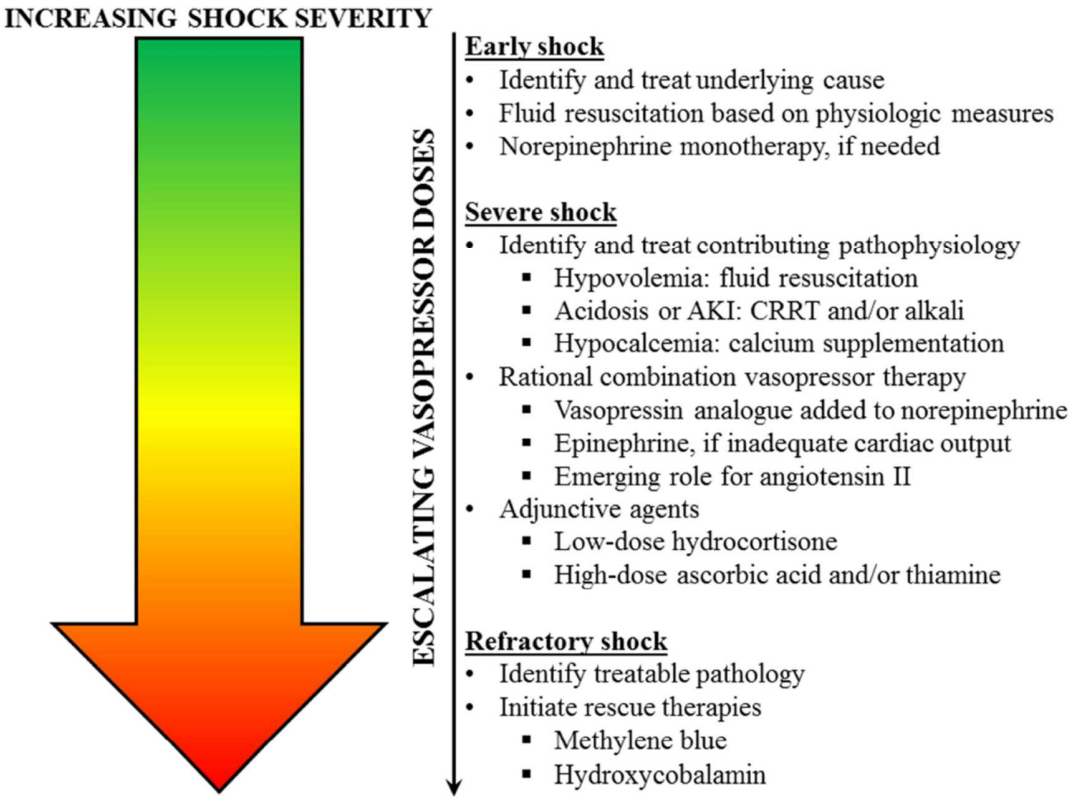



Figure 1 : Pathophysiology and diagnosis of shock states. Clinical assessment of various shock states begins with understanding that mean arterial pressure is the product of cardiac output and systemic vascular resistance. Signs of hypotension manifest as tissue hypoperfusion leading to a combination of delayed capillary refill time,  clammy and mottled extremities, elevated blood lactate and organ system changes such oliguria, altered mental status, and tachycardia.2 Categorization of the specific shock syndrome requires an assessment of volume status or cardiac filling pressures and cardiac output or surrogates such as mixed venous oxygenation2 [ Used with permission from Vincent JL, DeBacker D; NEJM 2013 ]

Figure 2 : A simplified approach to management of refractory vasodilatory shock [ Used with permission from : Jentzer JC et al., Chest 2018 ]


INCREASING SHOCK SEVERITY
ESCALATING VASOPRESSOR DOSES
Early shock
• Identify and treat underlying cause
• Fluid resuscitation based on physiologic measures
• Norepinephrine monotherapy, if needed
Severe shock
• Identify and treat contributing pathophysiology
▪ Hypovolemia: fluid resuscitation
▪ Acidosis or AKI: CRRT and/or alkali
▪ Hypocalcemia: calcium supplementation
• Rational combination vasopressor therapy
▪ Vasopressin analogue added to norepinephrine
▪ Epinephrine, if inadequate cardiac output
▪ Emerging role for angiotensin II
• Adjunctive agents
▪ Low-dose hydrocortisone
▪ High-dose ascorbic acid and/or thiamine
Refractory shock
• Identify treatable pathology
• Initiate rescue therapies
▪ Methylene blue
▪ Hydroxycobalamin

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